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(54) Title: METHODS FOR THE IDENTIFICATION OF AGENTS THAT MODULATE THE STRUCTURE AND PROCESSING OF A MEMBRANE BOUND PRECURSOR PROTEIN

(57) Abstract: The present invention provides methods for the screening and identification of agents from a large library of molecular structures that can alter the cleavage of a membrane protein of interest. Agents identified by the methods of the present invention that modify the cleavage of the membrane protein can be used in the treatment and prevention of diseases such as inflammation, diabetes, cancer, Alzheimer's disease, Parkinson's disease, and the like. The methods select for and identify effector agents that bind to the membrane protein of interest causing a structural change in the structure of the membrane protein in such a way that the efficiency of the cleavage of a secretase is modulated. Further, the methods are carried out in an in vivo system that provides for physiological conditions similar or identical to conditions for membrane protein processing. Agents can be selected for their ability to cause a decrease or increase the amount of secretase cleavage of the membrane protein.

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# INTERNATIONAL SEARCH REPORT

International application No.
PCT/US03/35289

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C12N 15/00; G01N 33/53, 33/567; A61K 49/00
US CL : 435/7.1, 7.21, 172.3; 530/350; 800/3

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 435/7.1, 7.21, 172.3; 530/350; 800/3

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EAST, MEDLINE

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|---|---|---|
| X<br>---<br>Y | US 6,440,698 B1 (GURNEY et al) 27 August 2002 (27.08.2002), column 10, lines 30-59; column 7, lines 34-46; column 35, line 7 to column 36, line 21; Table 4. | 1-7, 36-38, 46<br>---<br>15-35, 39-45, 47-54 |
| X<br>---<br>Y | HOOPER, N.M. et al. Membrane Protein Secretases. Biochem. J. 1997, Vol 321. pages 265-279, especially pages 268-272 (sections on (-amyloid precursor protein secretases and ACE secretase), and 275-276 (section on Secretase Assays, Whole Cell Assays). | 1-7, 36-38<br>---<br>15-35, 39-45, 47-54 |
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## C. (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|---|---|---|
| Y | US 6,420,110 B1 (GYURIS et al) 16 July 2002 (16.07.02) entire document, especially column 2, lines 31-33; column 19, lines 22-29; column 43, lines 22-24; column 18, lines 11-29; column 9, lines 36-37. | 21, 24, 28, 32, 45, 52 |
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